60/087,561, filed June 1, 1998, and is a continuing application of U.S.S.N. 09/127,926, filed July 31, 1998, and 09/058,459, filed April 10, 1998.--

Please replace the paragraph beginning at page 87, line 9, with the following rewritten paragraph:

--**Table 11.** *DEE determined optimal sequences for the core positions of Gβ1 as a function of* $\Delta h_{0.9}{}^{a}$–

Please replace the paragraph beginning at page 88, line 1, with the following rewritten paragraph:

--**Table 12.** *DEE determined optimal sequences for the core positions of Gβ1 as a function of* $\Delta h_{1.0}{}^{a}$–

Please replace the paragraph beginning at page 89, line 1, with the following rewritten paragraph:

--**Table 13.** *DEE determined optimal sequences for the core positions of Gβ1 as a function of* $\Delta \Omega_{0.9}{}^{a}$–

Please replace the paragraph beginning at page 90, line 1, with the following rewritten paragraph:

--**Table 14.** *DEE determined optimal sequences for the core positions of Gβ1 as a function of* $\Delta \theta_{0.9}{}^{a}$–

Please replace the paragraph beginning at page 91, line 1, with the following rewritten paragraph:

--**Table 15.** *DEE determined optimal sequences for the core positions of Gβ1 as a function of* $\Delta \sigma_{0.9}{}^{a}$--

Please replace the paragraph beginning at page 91, line 21, with the following rewritten paragraph:

A7

--The optimal sequence for the ten core positions of Gβ1 that is calculated using the native backbone (i.e., no perturbation) contains three conservative mutations relative to the wild-type sequence (Table 11). Y3F and V39I are likely the result of the hydrophobic surface area burial term in the scoring function. L7I reflects a bias in the rotamer library used for these calculations. The crystal structure of Gβ1 has the leucine at position 7 with a nearly eclipsed χ_2 of 111°. This strained χ_2 is unlikely to be an artifact of the structure determination since it is present in two crystal forms and a solution structure (Gronenborn et al., 1991; Gallagher et al., 1994). Our rotamer library does not contain eclipsed rotamers and no staggered leucine rotamers pack well at this position. Instead, the side-chain selection algorithm chose an isoleucine rotamer that conserves the χ_1 dihedral and is able to pack well. We expect the removal of the strained leucine rotamer to stabilize the protein, a prediction that is tested in the experimental section of this work. The sequences that result from varying individual super-secondary structure parameter values show two notable trends. Small variations in the parameter values tend to have little or no effect on the calculated sequences. For example, varying $\Delta h_{0.9}$ from -0.25 to -1.00 Å (Table 11) and $\Delta h_{1.0}$ from +0.25 to +1.25 Å (Table 2) has no effect on the calculated sequences which demonstrates the side-chain selection algorithm's tolerance to small variations in the initial backbone geometry. Large variations in the parameter values tend to result in greater sequence diversity. For example, $\Delta h_{1.0}$[+1.50Å] contains six out of ten possible mutations relative to Gβ1 (Table 12). The apparently anomalous result that occurs for $\Delta h_{0.9}$ at -1.25 and -1.50 Å, an increase in core volume, is explained by the observation that translating the helix towards the sheet plane results in creating a pocket of space in the vicinity of position 20 that ultimately leads to the observed A20V mutation.--

Please replace the paragraph beginning at page 92, line 10, with the following rewritten paragraph:

A8

--Experimental validation of the designed cores focused on seven of the Δh-series mutants which contain between three and six sequence changes relative to Gβ1. The designed sequences resulting from ΔΩ, Δθ and Δσ perturbations are, however, in many cases identical to various Δh-series sequences. Typical far UV circular dichroism (CD) spectra are shown in Figure 15. $\Delta h_{0.9}$[-1.00Å], $\Delta h_{0.9}$[0.00Å], $\Delta h_{0.9}$[+0.75Å] and $\Delta h_{0.9}$[+1.00Å] have CD spectra that are indistinguishable from that of Gβ1 while $\Delta h_{0.9}$[+1.50Å], $\Delta h_{1.0}$[+1.50Å] and $\Delta h_{0.9}$[-1.50Å] have CD spectra similar to that of Gβ1 suggesting that all of the mutants have a secondary structure content similar to the wild-type protein. Thermal melts monitored by CD are shown in Figure 16. All of the mutants have cooperative transitions with melting temperatures (T_m's) ranging from 53 °C for $\Delta h_{0.9}$[+1.50Å] to 91 °C for $\Delta h_{0.9}$[0.00Å] (Table 11). The T_m for Gβ1 is 85°C. The measured T_m's for $\Delta h_{0.9}$[-1.50Å] and $\Delta h_{0.9}$[+1.50Å] are for 56 residue proteins compared to 57 residue proteins in all other cases (see Methods and materials) which results in T_m's that are estimated to be about 2 °C higher than what would be expected for the corresponding 57 residue proteins based on the T_m difference between the 56 and 57 residue versions of Gβ1. The removal of the strained leucine at position seven (L7I) along with the increased hydrophobic burial generated by the Y3F and V39I mutations in $\Delta h_{0.9}$[0.00Å] result in a protein that is measurable more stable than wild-type Gβ1. The extent of chemical shift dispersion in the 1D ^{1}H NMR spectrum of each mutant was assessed to gauge each protein's degree of native-like character (Fig. 5). All of the mutants, except $\Delta h_{0.9}$[+1.50Å], have NMR spectra with chemical shift dispersion similar to that of Gβ1 suggesting that the proteins form well-ordered structures. $\Delta h_{0.9}$[+1.50Å] has a spectrum with broad peaks